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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Geuze and Melief

Serial No.: 09/011,167

Filed: 5 October, 1998

For: **CELL DERIVED ANTIGEN PRESENTING VESICLES**

Examiner: Martha Lubet

Art Unit: 1644

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

This response to the Restriction Requirement mailed 27 January, 2000 is submitted on or before the extended due date of 27 June, 2000, the time period for response having been extended by the attached Petition for Extension of Time for four (4) months. For the required fee, please see the attached Transmittal. Reconsideration is requested.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4, 6 and 13, drawn to an antigen presenting vesicle.
II. Claims 9, 11 and 12, drawn to a method of making or obtaining an antigen presenting vesicle.
III. Claim 10, drawn to method of stimulating T cell comprising contacting T cells with the antigen presenting vesicle of Group I.

Applicants elect Group I, claims drawn to an antigen presenting vesicle, and species A, antigen presenting vesicles comprising MHC class I molecules, with traverse. The Examiner writes that "the special technical feature linking the inventions of groups I and II does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a

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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first-class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on 6/27/2000
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contribution over the prior art. Rule 13.2 recites that "the expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions, *considered as a whole*, makes over the prior art". It is explicitly stated in the Melief '160 patent (col. 2, lines 10-20) that the crux of the invention disclosed therein is the use of antigen processing defective *cells* to increase the cell surface density of MHC class I molecules. The '160 specification was considered enabling to support claims specifically drawn to methods of using *whole cells* with this antigen processing defect. *When considered as a whole*, the '160 patent is strictly concerned with and only enabled for using *whole cells* having an antigen processing defect, and does not teach or suggest anything to the skilled artisan about the existence of antigen presenting vesicles obtainable from antigen presenting cells.

Although, as the Examiner has cited, Melief makes the sweeping statement in the '160 patent that "The invention is extended to all antigen presenting lipid bilayer carrying vehicles incorporating empty MHC molecules that can be loaded with exogenous peptides" (col. 5, lines 53-55), this specification does not enable the skilled artisan to practice such a broad invention, nor one that would be expected to be functional. In fact, Gueze and Melief teach in the instant specification that "it has been tried before to produce similar vesicles synthetically, for instance in the form of liposomes, but these attempts have sofar not been successful" (page 6, lines 7-9). Gueze and Melief also teach that because the vesicles automatically comprise all the necessary elements for antigen presentation, further analysis of the vesicles will result in a better understanding of which elements are essential for presentation and for reconstructing functional vesicles (page 6, lines 13-32). The novelty of the instant invention, *when considered as a whole*, is in the identification and isolation of antigen presenting vesicles obtainable from an antigen presenting cell. Claim 13 is specifically drawn to an antigen presenting vesicle that is *obtainable from an antigen presenting cell*. Claims 2-4 and 6 depend from Claim 13. Claim 1 was canceled in the preliminary amendment submitted with the application on 5 October, 1998.

The special technical features of Group I and Group II, directed to an antigen presenting vesicle and a method of obtaining an antigen presenting vesicle, respectively, define a contribution over the '160 patent, because the '160 specification does not teach or suggest or

mention anything even pertaining to the existence of MHC class I or class II enriched exosomes, or any other kind of vesicle obtainable from a cell. Applicants assume that the Examiner intends to discuss the relationship of Groups I and II in the second paragraph of page 3 of paper 10. Applicants teach different possible methods of producing antigen presenting vesicles obtainable from cells on page 6, lines 13-32, and importantly that synthetic vesicles functional for antigen presentation require other essential elements in addition to lipid bilayer and MHC molecules. As such, Applicants submit that the claims of Groups I and II are intimately related as directed to a composition comprising an antigen presenting vesicle and methods of specifically obtaining such a composition, and therefore deserve to be examined as part of a single application.

Concerning the species election, Applicants respectfully assert that the antigen presenting vesicles recited in the claims of Group I specifically relate to a single inventive concept with a uniquely shared technical feature, whether the vesicles contain enriched MHC class I or class II molecules. The unifying inventive concept is that exosomes with enriched MHC molecules (of either kind) present processed antigens to T cells. If the members of a Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. MPEP 803.02. Applicants respectfully submit that the two species in Claims 2-4, 6 and 13 are highly related and sufficiently few in number to avoid imposing an undue search and examination burden upon the Examiner, and such that they properly deserve to be examined together.

The only claim in Group III, Claim 10, is directed to a method of stimulating T cells using an antigen presenting vesicle as recited by the claims in Group I. The only intended use for the MHC-enriched cell-derived vesicles for the instant invention, as explicitly stated in the abstract and on page 7, lines 3-23, is for the purposes of vaccination, which necessarily requires T cell stimulation. The alternate uses for the MHC exosomes proposed by the Examiner of screening peptide MHC binding and eliciting anti-MHC antibodies also involve T cell stimulation. Assays for screening the ability of peptides to bind to MHC molecules oftentimes measure T cell stimulation as an indication of binding and production of antibodies

to any antigen necessarily requires T cell "help". Because the potential uses of MHC-enriched cell-derived vesicles are intimately related with T cell stimulation, Applicants respectfully assert that the claims of Groups I and III properly deserve to be examined in a single application.

In view of the foregoing reasons, Applicants respectfully request the Examiner to withdraw the three-way restriction of Claims 2-4, 6, and 9-13.

CONCLUSION

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 328-4400.

Respectfully submitted,

Dated: 27 June, 2000

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